IN THE CLAIMS:

The status of each claim that has been introduced in the above-referenced application is identified in the ensuing listing of the claims. This listing of the claims replaces all previously submitted claims listings.

1. (Currently amended) A biomolecular substrate comprising:

a core molecular backbone;

a first fluorescent dye covalently attached to said core molecular backbone; and

a second dye covalently attached to said core molecular backbone which, when said biomolecular substrate is not covalently modified, associates with said first fluorescent dye forming a quenched intramolecular dye dimer, fluorescence of which is at least partially quenched through a non-fluorescence resonance energy transfer mechanism, but which, when said biomolecular substrate is covalently modified without being cleaved, dissociates from said first fluorescent dye resulting in quenching of at least one of said first and second fluorescent dyes.

2. (Original) The biomolecular substrate of claim 1, wherein said second dye is a fluorescent dye.

3. (Original) The biomolecular substrate of claim 1 further comprising a first spacer segment included at a first terminus of said core molecular backbone.

4. (Original) The biomolecular substrate of claim 1 further comprising a first spacer segment included at a first terminus of said core molecular backbone and a second spacer segment included at a second terminus of said core molecular backbone.

5. (Original) The biomolecular substrate of claim 1, wherein said first fluorescent dye is selected from a group consisting of fluorescein, rhodamine, cyanine, Oregon Green, Texas Red, Lucifer Yellow, BODIPY, rhodol, coumarin, pyrene, eosin, erythrosin, napthalene,

pyridyloxazole, anthrancene, fluorescamine, acridine, benzofuran, anthranilic acid, aminobenzoic acid, N-methylisatoic acid, isoluminol, bezoxadiazole, carboxybenzoyl-quinoline-carboxyaldehyde, salicylate, bimane, phenathroline, Yellow Fluorescent Protein, and Green Fluorescent Protein.

6. (Original) The biomolecular substrate of claim 1, wherein said second dye is selected from a group consisting of fluorescein, rhodamine, cyanine, Oregon Green, Texas Red, Lucifer Yellow, BODIPY, rhodol, coumarin, pyrene, eosin, erythrosin, napthalene, pyridyloxazole, anthrancene, fluorescamine, acridine, benzofuran, anthranilic acid, aminobenzoic acid, N-methylisatoic acid, isoluminol, bezoxadiazole, carboxybenzoyl-quinoline-carboxyaldehyde, salicylate, bimane, phenathroline, Yellow Fluorescent Protein, and Green Fluorescent Protein.

7. (Original) The biomolecular substrate of claim 1, wherein said core molecular backbone comprises a molecule selected from a group consisting of a peptide, a protein, a nucleic acid, a sugar, a lipid, a receptor, and a biopolymer.

8. (Original) The biomolecular substrate of claim 1, wherein said core molecular backbone comprises an amino acid sequence.

9. (Original) The biomolecular substrate of claim 1, wherein said core molecular backbone includes a substrate determinant.

10. (Original) The biomolecular substrate of claim 1, wherein said core molecular backbone includes a protein kinase substrate.

11. (Original) The biomolecular substrate of claim 1, wherein said core molecular backbone includes a nucleotide sequence.

12. (Original) The biomolecular substrate of claim 1, wherein said core molecular backbone includes a lipid.

13. (Original) The biomolecular substrate of claim 1, wherein said core molecular backbone includes a biopolymer comprising a covalent combination of molecules selected from the group consisting of amino acids, nucleic acids, sugars, and lipids.

14. (Original) The protein kinase substrate of claim 1, wherein the core molecular backbone comprises a KID peptide sequence, the first fluorescent dye comprises fluorescein-succinimidyl ester, and the second dye comprises tetramethylrhodamine-maleimide.

15. (Currently amended) A method of assaying covalent biomolecular modification in a reaction comprising:

providing a sample with a biomolecular substrate comprising:

a core molecular backbone;

a first fluorescent dye covalently attached to said core molecular backbone; and

a second dye covalently attached to said core molecular backbone which, when said biomolecular substrate is not covalently modified, associates with said first fluorescent dye forming a quenched intramolecular dye dimer, fluorescence of which is at least partially quenched through a non-fluorescence resonance energy transfer mechanism, and affecting fluorescence or absorbance characteristics of said biomolecular substrate, but which dissociates from said first fluorescent dye when said biomolecular substrate is covalently modified without being cleaved;

introducing said biomolecular substrate to said sample; and

quantifying a resultant change in said fluorescence or absorbance characteristics of said biomolecular substrate.

16. (Original) The method of claim 15, wherein said biomolecular substrate is introduced into said living cells.

17. (Original) The method of claim 15, wherein said sample includes a drug targeting a specific process of covalent biomolecular modification.

18. (Original) The method of claim 16, wherein said sample includes a drug targeting a specific process of covalent biomolecular modification.

19. (Original) The method of claims 15, wherein said step of providing a biomolecular substrate comprises providing two or more different biomolecular substrates, each of said two or more biomolecular substrates being specific for different processes of covalent biomolecular modification and having unique and distinguishable spectral properties.

20. (Original) The method of claim 16, wherein said step of providing a biomolecular substrate comprises providing two or more different biomolecular substrates, each of said two or more biomolecular substrates being specific for different processes of covalent biomolecular modification and having unique and distinguishable spectral properties.

21. (Original) The method of claim 15, wherein the step of quantifying the resultant change in said fluorescence or absorbance characteristics of said biomolecular substrate comprises quantifying the resultant change in fluorescence or absorbance of said biomolecular substrate without separating biomolecular substrate which has been covalently modified from biomolecular substrate which has not been covalently modified.

22. (Original) The method of claim 16, wherein the step of quantifying the resultant change in fluorescence or absorbance characteristics of said biomolecular substrate comprises quantifying the resultant change in fluorescence or absorbance of said biomolecular substrate without separating biomolecular substrate which has been covalently modified from biomolecular substrate which has not been covalently modified.

23. (Previously presented) A method of assaying protein kinase activity comprising:

providing a biomolecular substrate comprising:

a KID peptide sequence;

a first molecule comprising a fluorescein or a rhodamine; and

a second molecule of comprising a rhodamine near the opposite end of said KID peptide sequence which, when said biomolecular substrate is not phosphorylated, associates with said first molecule forming an intramolecular dye dimer, fluorescence of which is at least partially quenched through a non-fluorescence resonance energy transfer mechanism, and dissociates from said first molecule when said biomolecular substrate is phosphorylated by a protein kinase to reduce said non-fluorescence resonance energy-transfer quenching;

providing a sample;

introducing said protein kinase substrate to said sample; and

quantifying a resultant change in fluorescence or absorbance of said biomolecular substrate.

24. (Original) The method of claim 23, wherein the step of quantifying the resultant change in fluorescence or absorbance of said biomolecular substrate comprises quantifying the resultant change in fluorescence or absorbance of said biomolecular substrate without separating biomolecular substrate which has been phosphorylated from biomolecular substrate which has not been phosphorylated.

25. (Currently amended) A method of identifying substrates of novel enzymes which catalyze covalent structural modifications of particular proteins or peptide sequences comprising:

gathering a combinatorial library of unique double-labeled substrates, said unique double-labeled substrates each comprising:

a particular, randomized core amino acid sequence;

a first fluorescent dye covalently attached to said particular, randomized core amino acid sequence; and

a second dye covalently attached to said particular, randomized core amino acid sequence which, when said unique double-labeled substrates are not covalently modified, associates with said first fluorescent dye forming a quenched intramolecular dye dimer, fluorescence of which is at least partially quenched through a non-fluorescence resonance energy transfer mechanism, and affecting the fluorescence or absorbance characteristics of said unique double-labeled substrates, but which dissociates from said first fluorescent dye when said unique double-labeled substrates are covalently modified without being cleaved;

systematically contacting each of said unique double-labeled substrates with a novel enzyme;

quantifying any change in fluorescence or absorbance characteristics of each of said unique double-labeled substrates;

selecting members of the library undergoing a fluorescence change or an absorbance change; and

determining the amino acid sequence of said selected members of the library.

26. (Currently amended) A kit comprising:

a container;

one or more different biomolecular substrates contained within said container, each of said one or more different biomolecular substrates comprising:

a core molecular backbone;

a first fluorescent dye associated with said core molecular backbone;

a second dye associated with said core molecular backbone which, when said biomolecular substrate is not covalently modified, associates with said first fluorescent dye forming a non-fluorescent intramolecular dye dimer at least partially through a ground state quenching mechanism, but which dissociates from said first fluorescent dye when said biomolecular substrate is catalytically or non-catalytically covalently modified without being cleaved to reduce quenching by said ground state interaction; and

a sample of enzyme standard with which to standardize the assay.

27. (Currently amended) A method of identifying substrates of novel enzymes which catalyze covalent structural modifications of particular nucleic acids comprising:

gathering a combinatorial library of unique double-labeled substrates, said unique double-labeled substrates each comprising:

a particular, randomized core nucleic acid sequence;

a first fluorescent dye associated with said particular, randomized core nucleic acid sequence; and

a second dye associated with said particular, randomized core nucleic acid sequence which, when said unique double-labeled substrates are not covalently modified, associates with said first fluorescent dye forming a quenched intramolecular dye dimer, fluorescence of which is at least partially quenched through a non-fluorescence resonance energy transfer mechanism, and affecting the fluorescence or absorbance characteristics of said unique double-labeled substrates, but which dissociates from said first fluorescent dye when said unique double-labeled substrates are covalently modified without being cleaved;

systematically contacting each of said unique double-labeled substrates with a novel enzyme;

quantifying any change in fluorescence or absorbance of each of said unique double-labeled substrates;

selecting members of the library undergoing a fluorescence or absorbance change; and

determining the nucleotide sequence of said selected members of the library.